Hepatorenal Syndrome

AKI in cirrhosis is not automatically HRS · It is a diagnosis of exclusion with a two-day albumin test built in

ALBUMIN 1 g/kg
× 2 days, then judge

WHAT IT ACTUALLY IS *a functional kidney problem caused by the circulation, not by the kidney*

THE MECHANISM

Portal hypertension drives splanchnic arterial vasodilatation, so the effective arterial blood volume falls despite obvious total-body fluid overload. The **renin-angiotensin, sympathetic and vasopressin systems switch on**, producing **intense renal vasoconstriction**.

THE KIDNEYS ARE NORMAL

There is no structural damage — which is why the urine is bland, why kidneys from HRS donors work normally when transplanted, and why **the syndrome reverses when the circulation is corrected or the liver is replaced**. Treat the circulation, not the kidney.

THE TWO FORMS

HRS-AKI (formerly type 1) is a **rapid rise in creatinine over days**, usually with a precipitant, and carries a very poor prognosis untreated. **HRS-NAKI** (formerly type 2) is a **slower decline with diuretic-refractory ascites**.

THE DIAGNOSTIC CRITERIA *the fixed creatinine cutoff was removed so treatment can start earlier*

Criterion	Detail
Cirrhosis with ascites	The syndrome occurs in **decompensated cirrhosis with ascites**, and also in acute liver failure and alcohol-related hepatitis.
AKI is present	A **creatinine rise of 0.3 mg/dL or more within 48 hours, or 50% or more from baseline within 7 days**. **The old requirement for a creatinine above 2.5 mg/dL was abandoned**, because waiting for that number meant treating far too late. **Do not wait for a threshold value before acting.**
No response to the albumin challenge	**Withdraw diuretics and give albumin 1 g/kg daily (up to 100 g) for 2 consecutive days. Persisting AKI after that is the defining feature** — it simultaneously excludes simple hypovolemia and treats it. This step is frequently skipped or under-dosed.
No shock	Hypotension requiring vasopressors from sepsis or hemorrhage points to **acute tubular necrosis**, which behaves and is managed differently.
No nephrotoxins	No recent **NSAIDs, aminoglycosides, or iodinated contrast**. Review the chart carefully; a single NSAID course is a classic and preventable precipitant.
No structural kidney injury	**Proteinuria below 500 mg/day, fewer than 50 red cells per high-power field, and a normal renal ultrasound.** Significant proteinuria or an active sediment means **glomerular disease** — think hepatitis B or C associated nephropathy, or IgA nephropathy in alcohol-related cirrhosis.

EXCLUDE THE COMMONER CAUSES FIRST *most AKI in cirrhosis is not HRS*

Cause	Clue and action
Hypovolemia	**The commonest cause overall.** Over-diuresis, large-volume paracentesis without adequate albumin cover, vomiting, diarrhea, and **lactulose-induced losses**. **Responds to stopping diuretics and giving volume** — which is exactly what the albumin challenge tests.
Infection	**Do a diagnostic ascitic tap on every cirrhotic patient with AKI**, whatever the temperature. **Spontaneous bacterial peritonitis precipitates HRS** and is frequently afebrile and asymptomatic. Also look for urinary, chest and skin sources.
Gastrointestinal bleeding	Variceal or otherwise, causing hypovolemia and renal hypoperfusion. Look for melaena and a rising urea disproportionate to the creatinine.
Acute tubular necrosis	Follows prolonged hypotension, sepsis or nephrotoxins. **Granular casts and a higher urinary sodium** support it, though these are unreliable in cirrhosis. It does not respond to vasoconstrictors.
Obstruction	**Ultrasound every patient**. Cheap, fast, and occasionally the whole answer.

TREAT *vasoconstrictor plus albumin, and refer for transplant in parallel*

1. **Stop diuretics, beta-blockers if hypotensive, NSAIDs and any nephrotoxin**, and treat the precipitant — drain and treat infection, control bleeding. **Give albumin cover with large-volume paracentesis** and treat spontaneous bacterial peritonitis with **albumin as well as antibiotics**, which reduces both HRS and mortality.
2. **Terlipressin plus albumin is first-line.** The vasoconstrictor reverses splanchnic vasodilatation and restores renal perfusion. **Reversal of HRS is achieved in a substantial minority, though without a clear survival benefit**, so the aim is to buy renal recovery and a bridge to transplant.
3. **Select patients carefully for terlipressin. Respiratory failure is the key harm** — avoid in significant hypoxemia or advanced cardiopulmonary disease, and monitor oxygenation closely. Also watch for **ischemic complications** in peripheral, mesenteric and coronary beds, and for hyponatremia.
4. **Where terlipressin is unavailable or contraindicated, use norepinephrine** with albumin in a monitored setting, or **midodrine with octreotide and albumin** outside critical care, which is less effective but usable on a ward.
5. **Refer for liver transplantation early — it is the only definitive treatment. Renal replacement therapy is a bridge** for transplant candidates or where recovery is plausible, not a destination in a patient who is not a candidate. **TIPS** helps selected patients. **Have the ceiling-of-care conversation in parallel**, because untreated HRS-AKI in a non-transplant candidate has a very short prognosis.

PEARLS & PITFALLS

- **Terlipressin dosing: 1 mg IV every 6 h with albumin**, escalating to **2 mg every 6 h if creatinine has not fallen by 25% by day 3**. **Monitor oxygen saturation closely**: respiratory failure is the dose-limiting toxicity, and hypoxemia at baseline is a reason not to start.
- **Tap the ascites in every cirrhotic patient with AKI.** Spontaneous bacterial peritonitis is often silent and precipitates HRS.
- **Give the full albumin challenge before diagnosing HRS** — 1 g/kg for 2 days with diuretics stopped. Under-dosing it mislabels simple hypovolemia.
- **Do not wait for a threshold creatinine.** That cutoff was deliberately removed so treatment could start earlier.
- **Check for NSAIDs.** A single course is a classic, entirely preventable precipitant.
- **Cover large-volume paracentesis with albumin**, and give albumin alongside antibiotics in SBP — both prevent HRS.
- **Watch oxygenation on terlipressin.** Respiratory failure is its most important harm and the reason for careful selection.

References: International Club of Ascites revised consensus definitions of AKI and hepatorenal syndrome in cirrhosis · EASL clinical practice guidelines on decompensated cirrhosis · AASLD guidance on ascites and hepatorenal syndrome · CONFIRM (terlipressin in HRS-AKI).